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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/910,388	07/20/2001	Lawrence L. Kunz	10177-211-999	1690

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EXAMINER	
VIVLEMORE, TRACY ANN	

ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
07/07/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/910,388	KUNZ, LAWRENCE L.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50,52-55,58 and 59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50,52-55,58 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/22/08 and 4/23/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection or objection not reiterated in this Action is withdrawn.

This application has been assigned to a different examiner.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 23, 2009 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 50, 52-55 and 59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application

was filed, had possession of the claimed invention. This is a written description rejection.

The claims are directed to a method of reducing restenosis by local administration of a cytostatic amount of a therapeutic agent that inhibits vascular smooth muscle cell activity without killing the cell. The claimed therapeutic agents include modified toxins, such as a modified diphtheria toxin and a modified ricin toxin, and *Pseudomonas exotoxin*.

The instant specification contemplates toxins and modified toxins as suitable therapeutic agents at paragraph 54 and mentions modified diphtheria and ricin toxins as examples of metabolic inhibitors at paragraph 57, but the specification provides no further description of any toxins or modified toxins. For example, there is no description in the specification of how a toxin is to be modified in order to produce a modified toxin that is capable of acting as a therapeutic agent in the context of the claimed invention. The specification provides no disclosure of the structural features of modified toxins that correlate to the claimed function of reducing restenosis by inhibiting smooth muscle cell activity without killing the cell.

While *Pseudomonas exotoxin* and modified diptheria and ricin toxins were known at the time of invention and had been used as therapeutic agents against diseases such as cancer, these toxins were in fact used for their cytotoxic effects in order to kill the diseased cells (see, for example, Pastan et al., Annual Review of Biochemistry 1992). The prior art does not supply the description missing from the instant specification of a correlation between the structure of a modified toxin and the function of inhibiting an activity of cells without killing the cell.

In order for the written description provision of 35 USC 112, first paragraph to be satisfied, applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed. For example, MPEP 2163 states in part,

> "An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.")."

The skilled artisan cannot envision the detailed structure of the encompassed modified toxins that act to inhibit activity of a cell without killing the cell, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention.

Therefore, the full breadth of modified toxins encompassed by the claims does not meet the written description provision of 35 USC 112, first paragraph.

Response to Arguments

The claim amendments submitted 4/23/09 have overcome the previous grounds of rejection for lack of written description, but have introduced new issues as set forth above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 50, 52-55, 58 and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over March et al. (US 5,171,217), Khan et al. (US 5,413,797), Baker (US 4,919,939), Shaw (US 4,233,968) and Haugwitz et al. (US 4,942,184)

The claims are directed to methods of reducing restenosis following a vascular surgical procedure comprising locally administering a biocompatible, non-biodegradable sustained release dosage form comprising a therapeutic agent in an amount that inhibits a vascular smooth muscle cell activity without killing the cell. In specific embodiments the surgical procedure is stent placement or angioplasty, the administration is direct to vascular smooth muscle tissue and occurs during or after the procedure, the agent is taxol or taxotere and the dosage form is a microparticle.

March et al. teach (see columns 1-3) that studies have indicated that angioplasty may produce endothelial denudation, injury to the vascular wall and rupture of the vasa vasorum, and that the accompanying uncontrolled proliferation of smooth muscle cells within the arterial wall has been widely implicated as a prominent factor in the resulting restenosis. March et al. teach methods and compositions for delivering a drug to an affected intramural site for sustained release in conjunction with procedures such as angioplasty or stent placement. The drug is carried by microparticles of a

physiologically-compatible, biodegradable polymer and injected under directed pressure into the wall of a body vessel in the region of the affected site. March et al. teach that administration of a smooth muscle cell inhibitor may precede, attend or follow angioplasty. Delivery can be by catheter or other injection device. One particular class of therapeutic agents taught by March et al. is anti-mitotic agents.

March et al. do not teach non-biodegradable polymers in their sustained-release compositions, but at the time the invention was made it was well known to those of ordinary skill in the art that both biodegradable and non-biodegradable polymers were routinely used in such dosage forms. This concept is illustrated by the teachings of Baker, Shaw and Khan et al., who each teach polymeric drug compositions where the polymer can be either biodegradable or non-biodegradable. Khan et al. further teach at column 1, lines 54-64 that one way of controlling blood levels of a compound is to administer it in the form of a polymeric matrix that releases compound as a function of polymer degradation and/or drug diffusion and that both biodegradable and non-biodegradable polymers have been used for such compositions. The release is controlled by selection of the appropriate polymer, encapsulation conditions, and drug loading and excipients.

Haugwitz et al. teach that taxol is an anti-mitotic compound (see column 1, lines 14-30).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to produce the sustained release compositions taught by March et al. as suitable for treatment of restenosis following angioplasty or stent placement using a non-biodegradable polymer. One of ordinary skill in the art would recognize that use

of a non-biodegradable polymer in place of a biodegradable polymer is a matter of design choice because those in the art were aware based on the teachings of Shaw, Baker and Khan that these types of polymers were routinely used interchangeably in drug delivery formulations. It would further have been obvious to use taxol as the therapeutic agent in the method of March et al. because March et al. explicitly teach that anti-mitotic agents are a suitable class of agents and Haugwitz et al. teach that taxol is an anti-mitotic agent. The use of a cytostatic amount of taxol that does not kill cells is a matter of routine optimization of dosage. See MPEP 2144.05 II: "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955).

Thus, the invention of claims 50, 52-55, 58 and 59 would have been obvious, as a whole, at the time the invention was made.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now

contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

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